CLAIMS

We claim:

1. A targeting construct comprising:
   (a) a first polynucleotide sequence homologous to a RORγ gene;
   (b) a second polynucleotide sequence homologous to the RORγ gene; and
   (c) a selectable marker.
2. The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
3. A method of producing a targeting construct, the method comprising:
   (a) providing a first polynucleotide sequence homologous to a RORγ gene;
   (b) providing a second polynucleotide sequence homologous to the RORγ;
   (c) providing a selectable marker; and
   (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
4. A method of producing a targeting construct, the method comprising:
   (a) providing a polynucleotide comprising a first sequence homologous to a first region of a RORγ gene and a second sequence homologous to a second region of a RORγ gene;
   (b) inserting a positive selection marker in between the first and second sequences to form the targeting construct.
5. A cell comprising a disruption in a RORγ gene.
6. The cell of claim 5, wherein the cell is a murine cell.
7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.
8. A non-human transgenic animal comprising a disruption in a RORγ gene.
9. A cell derived from the non-human transgenic animal of claim 8.
10. A method of producing a transgenic mouse comprising a disruption in a RORγ gene, the method comprising:
    (a) introducing the targeting construct of claim 1 into a cell;
    (b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse.

11. A method of identifying an agent that modulates the expression of a RORγ, the method comprising:

(a) providing a non-human transgenic animal comprising a disruption in a RORγ gene;

(b) administering an agent to the non-human transgenic animal; and

(c) determining whether the expression of RORγ in the non-human transgenic animal is modulated.

12. A method of identifying an agent that modulates the function of a RORγ, the method comprising:

(a) providing a non-human transgenic animal comprising a disruption in a RORγ gene;

(b) administering an agent to the non-human transgenic animal; and

(c) determining whether the function of the disrupted RORγ gene in the non-human transgenic animal is modulated.

13. A method of identifying an agent that modulates the expression of RORγ, the method comprising:

(a) providing a cell comprising a disruption in a RORγ gene;

(b) contacting the cell with an agent; and

(c) determining whether expression of the RORγ is modulated.

14. A method of identifying an agent that modulates the function of a RORγ gene, the method comprising:

(a) providing a cell comprising a disruption in a RORγ gene;

(b) contacting the cell with an agent; and

(c) determining whether the function of the RORγ gene is modulated.

15. The method of claim 13 or claim 14, wherein the cell is derived from the non-human transgenic animal of claim 8.

16. An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.

17. A transgenic mouse comprising a disruption in a RORγ gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: a spleen abnormality, a kidney abnormality ~~a spleen abnormality~~ a liver abnormality, an abnormality of the thymus, an abnormality in the lymph nodes, an abnormality in the lymphocytes, an abnormality in the bone marrow, or an abnormality in the bones.

18. The transgenic mouse of claim 17, wherein the spleen abnormality is increased weight of the spleen relative to a wild-type mouse.

19. The transgenic mouse of claim 17, wherein the spleen abnormality is increased size of the spleen relative to a wild-type mouse.

20. The transgenic mouse of claim 17, wherein the spleen abnormality is an increased spleen to body weight ratio relative to a wild-type mouse.

21. The transgenic mouse of claim 17, wherein the kidney abnormality is increased weight of the kidney relative to a wild-type mouse.

22. The transgenic mouse of claim 17, wherein the kidney abnormality is increased size of the kidney relative to a wild-type mouse.

23. The transgenic mouse of claim 17, wherein the kidney abnormality is an increased kidney to body weight ratio relative to a wild-type mouse.

24. The transgenic mouse of claim 17, wherein the liver abnormality is increased weight of the liver relative to a wild-type mouse.

25. The transgenic mouse of claim 17, wherein the liver abnormality is increased size of the liver relative to a wild-type mouse.

26. The transgenic mouse of claim 17, wherein liver abnormality is an increased liver to body weight ratio relative to a wild-type mouse.

27. The transgenic mouse of claim 17, wherein the thymus abnormality is increased weight of the thymus relative to a wild-type mouse.

28. The transgenic mouse of claim 17, wherein the thymus abnormality is increased size of the thymus relative to a wild-type mouse.

29. The transgenic mouse of claim 17, wherein the thymus abnormality is an increased thymus to body weight ratio relative to a wild-type mouse.

30. The transgenic mouse of claim 17, wherein the abnormality of the thymus is thymic cortical expansion and medullary reduction relative to a wild-type mouse.

31. The transgenic mouse of claim 17, wherein the abnormality of the lymph nodes is depletion of lymph nodes relative to a wild-type mouse.

32. The transgenic mouse of claim 17, wherein the abnormality of the lymph nodes is absence of lymph nodes.

33. The transgenic mouse of claim 17, wherein the abnormality of the lymph nodes is depletion of gut associated lymphoid tissue ratio relative to a wild-type mouse.

34. The transgenic mouse of claim 17, wherein the abnormality lymphocytes comprises lymphoid infiltrates.

35. The transgenic mouse of claim 17, wherein the abnormality lymphocytes is consistent with lymphoma.

36. The transgenic mouse of claim 35, further comprising at least one of the following symptoms of disease: poor grooming, hypoactivity, increased thoracic girth, and increased abdominal girth, hepatosplenomegaly, enlarged thymus, ascites, weakness, squinting, hunching, cachexia, lethargy, and impaired respiration.

37. The transgenic mouse of claim 17, wherein the bone marrow is pale.

38. The transgenic mouse of claim 17, wherein the abnormality of the bones is brittleness.

39. The transgenic mouse of claim 17, wherein the abnormality of the bones is attached white masses.

40. A method of producing a transgenic mouse comprising a disruption in a RORγ gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: a spleen abnormality, a kidney abnormality, ~~a spleen abnormality~~ a liver abnormality, an abnormality of the thymus, an abnormality in the lymph nodes, an abnormality in the lymphocytes, an abnormality in the bone marrow, or an abnormality in the bones, the method comprising:

(a) introducing a RORγ gene targeting construct into a cell;

(b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse comprising a disruption in a RORγ gene.

41. A cell derived from the transgenic mouse of claim 17 or claim 40.

42. A method of identifying an agent that ameliorates a phenotype associated with a disruption in a RORγ gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a disruption in a RORγ gene; and

(b) determining whether the agent ameliorates at least one of the following phenotypes: a spleen abnormality, a kidney abnormality, ~~a spleen abnormality~~ a liver abnormality, an abnormality of the thymus, an abnormality in the lymph nodes, an abnormality in the lymphocytes, an abnormality in the bone marrow, or an abnormality in the bones.

43. A method of identifying an agent that ameliorates a phenotype associated with a disruption in a RORγ gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a disruption in a RORγ gene; and

(b) determining whether the agent ameliorates at least one of the following phenotypes: elevated serum alanine aminotransferase, elevated serum alkaline phosphatases, elevated serum aspartate aminotransferase, elevated blood urea nitrogen, and elevated blood phosphorus.

44. A method of identifying an agent that ameliorates a phenotype associated with a disruption in a RORγ gene, the method comprising:

(a) administering an agent to the transgenic mouse comprising a disruption in a RORγ gene; and

(b) determining whether the agent modulates RORγ expression in the transgenic mouse, wherein the agent has an effect on at least one of the following symptoms of disease: poor grooming, hypoactivity, increased thoracic girth, and increased abdominal girth, hepatosplenomegaly, enlarged thymus, ascites, weakness, squinting, hunching, cachexis, lethargy, and impaired respiration.

45. A method of identifying an agent that modulates RORγ gene function, the method comprising:

(a) providing a cell comprising a disruption in a RORγ gene;

(b) contacting the cell with an agent; and

(c) determining whether the agent modulates RORγ gene function, wherein the agent modulates a phenotype associated with a disruption in a RORγ gene.

46. The method of claim 45, wherein the phenotype comprises at least one of the following: a spleen abnormality, a kidney abnormality, ~~a spleen abnormality~~ a liver abnormality, an abnormality of the thymus, an abnormality in the lymph nodes, an abnormality in the lymphocytes, an abnormality in the bone marrow, or an abnormality in the bones.

47. The method of claim 45, wherein the phenotype comprises lymphoma.

48. An agent identified by the method of claim 42, claim 43,claim 44, or claim 45.

49. A transgenic mouse comprising a disruption in a RORγ gene, wherein the transgenic mouse exhibits lymphoma.